

CLAIMS:

1. A method for producing MR contrast agent, the method comprising the steps of:
-*obtaining* (100) a solution in a solvent of a hydrogenatable, unsaturated substrate
5 compound and a catalyst for the hydrogenation of a substrate compound, wherein the
substrate compound comprises imaging nuclei;
-*hydrogenating* (110) the substrate with hydrogen gas (H₂) enriched in para-
hydrogen (p-¹H₂) to form a hydrogenated contrast agent;
-*exposing* (120) the contrast agent to a oscillating magnetic field in combination with
10 a stationary magnetic field for enhancing the contrasting effects of the contrast agent
adapted for use in an MR application.
2. The method according to claim 1 **wherein** the oscillating magnetic field is oscillating
with a frequency within the region of radio frequencies (e.g from around 10 Hz to
several GHz).
- 15 3. The method according to claim 1 **wherein** the oscillating magnetic field is oscillating
with a frequency in the interval 5kHz to 500 MHz.
4. The method according to any of claim 2 **wherein** the step of exposure to the
oscillating magnetic field in combination with the stationary magnetic field is
performed during the step of hydrogenation, wherein the step of exposure is
20 performed for reducing the relaxation of the spin system of the contrast agent,
whereby the contrasting effects of the contrast agent is enhanced.
5. The method according to claim 2 **wherein** the step of exposure to the oscillating
magnetic field in combination with the stationary magnetic field is to be performed
after the step of hydrogenation, the step of exposure is performed for enhancing the
25 degree of polarization of an imaging nuclei of the contrast agent, whereby the
contrasting effects of the contrast agent is enhanced.
6. The method according to claim 5 **wherein** the step of exposure to the oscillating
magnetic field in combination with the stationary magnetic field comprises exposing
the contrast agent to at least one series of pulses of the oscillating magnetic field (rf-
30 pulse).

7. The method according to claim 6 wherein the exposing step comprises:
 -*applying* (420) a first series of pulses of the Larmor frequency of the imaging nuclei of the hydrogenated contrast agent and delays between the pulses, the first series adapted to bring the system into a state consisting of a zero quantum coherence involving the protons and the imaging nuclei;
 -*applying* (430-480) a second series of pulses of the Larmor frequency of the imaging nuclei of the hydrogenated contrast agent and delays between the pulses, the second series adapted to give a progressive build up of carbon polarization in the direction of the external field axis.
8. The method according to claim 6 wherein the exposing step comprises:
 (a) -*applying* (420) a series of 180°_x pulses followed by delays(t_i) on the imaging nuclei;
 (b) -*applying* (430) a 90°_y pulse on carbon;
 (c) -*waiting* (440) for $t/2$ s;
 (d) -Optionally *applying* (450) simultaneous 180°_x pulses on hydrogen and the imaging nuclei in order to compensate for the effect of field inhomogeneities;
 (e) -Optionally *waiting* (460) for $t/2$ s;
 (f) -*applying* (470) a pulse with an angle ϕ_x on the imaging nuclei;
 (g) -Optionally *repeating* steps c to f to produce a progressive build up of the imaging nuclei polarization in the direction of the external field axis, wherein the angle ϕ_x may be different in each repetition.
9. The method according to claim 6 wherein the exposing step comprises:
 -*applying* (520) a first series of pulses of the Larmor frequency of the imaging nuclei of the hydrogenated contrast agent and delays between the pulses, the first series adapted to bring the system into a state consisting of a zero quantum coherence involving the protons and the imaging nuclei;
 -*applying* (530-540) a second series of pulses and delays between the pulses comprising of pulses of the Larmor frequency of the imaging nuclei of the hydrogenated contrast agent alternated with pulses of the Larmor frequency of the hydrogen of the hydrogenated contrast agent, the second series adapted to transform a two-proton-double quantum coherence into a three-spin coherence involving the spins of the imaging nuclei;
 -*applying* (570) simultaneous 90°_y and 90°_ϕ pulses on the imaging nuclei and

hydrogen, respectively, adapted for producing a transverse polarization of the imaging nuclei.

10. The method according to claim 6 **wherein** the exposing step comprises:
 - applying* (520) a series of 180°_x pulses followed by delays t_1 on the imaging nuclei;
 - 5 -*applying* (530) a 90°_y pulse on hydrogen;
 - waiting* (540) for $t_2/2$ s;
 - optionally applying* (550) simultaneous 180°_x pulses on hydrogen and the imaging nuclei in order to compensate for the effect of field inhomogeneities;
 - optionally waiting* (560) for $t_2/2$ s;
 - 10 -*applying* simultaneous (570) 90°_y and 90°_ϕ pulses on the imaging nuclei and hydrogen;
 - waiting* (580) for $t_3/2$ s;
 - applying* (585) simultaneous 180°_x pulses on the imaging nuclei and hydrogen;
 - waiting* (590) for $t_3/2$ s;
 - 15 -*applying* (595) a -90°_y pulse on carbon.
11. Method according to any of claims 7-10 **wherein** one or more of the radiofrequency pulses is either composite or modulated in amplitude, phase or frequency or any combination thereof.
12. Apparatus for producing MR contrast agent, the apparatus comprising a magnetic
20 treatment unit (240) adapted for magnetic treatment of the contrast agent,
 characterised in that the magnetic treatment unit (240) comprises means for producing an oscillating magnetic field and means for producing a stationary magnetic field.
13. Apparatus according to claim 11 **wherein** said magnetic treatment unit (240) is
25 combined with a hydrogenation reactor 210.
14. Apparatus according to claim 12 or 13 **wherein** said magnetic treatment unit (240) comprises essentially the magnetic system of a NMR spectrometer.
15. Apparatus according to claim 14 **wherein** said magnetic system of a NMR
30 spectrometer additionally are used for analyzing the produced contrast agent with NMR spectroscopy.

16. Apparatus according to claim 12 or 13 wherein said magnetic treatment unit (240) comprises a Helmholtz pair (360) for producing the stationary magnetic field and a NMR coil (360) for producing the oscillating magnetic field.
- 5 17. A computer program product directly loadable into the internal memory of a processing means within a processing unit for controlling the method and apparatus for producing MR contrast agent, comprising the software code means adapted for controlling the steps of any of the claims 1 to 11.
- 10 18. A computer program product stored on a computer usable medium, comprising a readable program adapted for causing a processing means, in a processing unit for controlling the method and apparatus for producing MR contrast agent, to control an execution of the steps of any of the claims 1 to 11.